13. Armstrong D, Gold JWM, Dryjanski J, et al: Treatment of infections in patients with the acquired immunodeficiency syndrome. Ann Intern Med 1985; 103:738-743

14. Young LS: Mycobacterium avium complex infection. J Infect Dis 1988; 157:863-867

15. Hawkins CC, Gold JWM, Estella W, et al: Mycobacterium avium complex infections in patients with the acquired immunodeficiency syndrome. Ann Intern Med 1986; 105:184-188

16. Potter DA, Danforth DN, Macher AM, Longo DL, Stewart L, Masur H: Evaluation of abdominal pain in the AIDS patient. Ann Surg 1984; 199:332-339

17. Wilson SE, Robinson G, Williams RA, et al: Acquired immune deficiency syndrome (AIDS)—Indications for abdominal surgery, pathology, and outcome. Ann Surg 1989; 210:428-434

Lactic Acidosis in a Patient With Multiple Myeloma

BARRY A. MIZOCK, MD
JORGE N. GLASS, MD
Chicago, Illinois

TYPE B LACTIC ACIDOSIS has been described in association with a variety of hematologic malignant neoplasms and solid tumors. We report the first case of type B lactic acidosis occurring in a patient with multiple myeloma. We also review functional abnormalities relevant to the genesis of lactic acidosis in patients with malignancy and those with multiple myeloma.

Report of a Case

The patient, a 60-year-old woman, was admitted because of vomiting and weakness for four days. She had had multiple myeloma for three years with diffuse lytic lesions in the humerus, skull, and thoracic spine. She received radiation therapy (50 Gy [5,000 rads]) in February 1993 for spinal cord compression and received additional courses of radiation therapy in July 1993. She had also been treated with several cycles of chemotherapy consisting of melphalan, cyclophosphamide, and prednisone. Her myeloma was deemed to be unresponsive to therapy. Outpatient medications included acetaminophen, dexamethasone sulfate, fluconazole, and sulfamethoxazole.

On admission the patient appeared nontoxic. Her blood pressure was 170/82 mm of mercury, her heart rate was 120 beats per minute, respirations were 20 per minute, and her temperature was 36.9°C (98.5°F). Her mucous membranes were dry. Nodules were noted over the skull diffusely. Pain was elicited to palpation of the left upper chest wall. The results of the physical examination were otherwise unremarkable. Admitting laboratory test values included the following: leukocyte count 10.7 $\times$ 10^9 per liter (10,700 per mm^3), hemoglobin 115 grams per liter (11.5 grams per dl), and platelet count 229 $\times$ 10^9 per liter (229,000 per mm^3). Serum sodium level was 137 mmol per liter (137 mEq per liter), potassium 5.1 mmol per liter (5.1 mEq per liter), chloride 104 mmol per liter (104 mEq per liter), carbon dioxide 12 mmol per liter (12 mEq per liter), anion gap 21, total calcium 6.1 mmol per liter (12.3 mEq per liter), urea nitrogen 15.4 mmol per liter (43 mg per dl), creatinine 88 μmol per liter (1.0 mg per dl), and glucose 6.2 mmol per liter (112 mg per dl). Liver function test values were normal. A prothrombin time was 11.2 seconds. Arterial blood gas determinations with the patient breathing room air were as follows: pH 7.35, P_{CO_2} 20 mm of mercury, P_{O_2} 100 mm of mercury, bicarbonate 10.8 mmol per liter (10.8 mEq per liter), and arterial oxygen saturation 95%. An arterial lactate level was 8.5 mmol per liter. A urinalysis was normal. The chest x-ray film showed a small left pleural effusion. Gram's stain of a sputum specimen was unremarkable.

The cause of the increase in lactate was not obvious. The patient was never observed to have seizure activity. The presence of occult tissue hypoperfusion was considered, and intravenous fluids were administered. In addition, a regimen of broad-spectrum antibiotics was started empirically for possible sepsis. When the elevated blood lactate level did not diminish with hydration, a pulmonary artery catheter was inserted to further define the perfusion status. The cardiac output was 8.7 liters per minute, the systemic vascular resistance was 746 dynes • second • cm^{-5}, the pulmonary artery pressure was 28/4 mm of mercury, the pulmonary artery wedge pressure was 9 mm of mercury, right atrial pressure was 6 mm of mercury, mixed venous oxygen tension was 42.4 mm of mercury, percentage of saturated venous oxygen was 78.6%, oxygen extraction ratio was 0.2, and the lactate level was 6.6 mmol per liter. A course of thiamine was empirically administered but had no effect on the lactate level. The patient remained afebrile; the leukocyte count ranged from 5.3 to 10 $\times$ 10^9 per liter. Antibiotic therapy was stopped after eight days. Culture of urine, blood, and sputum specimens was negative for pathogens. The blood lactate concentration continued to be elevated throughout her hospital course and was 9.5 mmol per liter at the time of her discharge from hospital. Radiation therapy was planned on an outpatient basis. She was readmitted three weeks later with recurrent hypercalcemia and weakness, and her blood lactate concentration remained elevated throughout this admission. She was discharged home on a regimen of calcitonin.

Discussion

The most common cause of lactic acidosis in patients with malignant neoplasms is tissue hypoperfusion due to hypovolemia, sepsis, or cardiac dysfunction.[1] Lactic acidosis occurring in patients with clinical evidence of poor tissue perfusion or oxygenation (such as hypotension, cyanosis, cool extremities) is classified in the Cohen and Woods system as type A lactic acidosis.[2] Tissue hypoperfusion was thought not to be present in our patient based on the normal hemodynamic profile, negative cultures, and persistent lactic acidosis at the time of discharge.

(Mizock BA, Glass JN: Lactic acidosis in a patient with multiple myeloma. West J Med 1994; 161:417-418)

From the Division of Critical Care Medicine and Department of Medicine, Cook County Hospital, and the University of Health Sciences/Chicago Medical School, Chicago, Illinois.

Reprint requests to Barry A. Mizock, MD, Department of Medicine, Cook County Hospital, 1835 West Harrison, Chicago, IL 60612.

It was first noted in 1961 that lactic acidosis could occur in patients in whom neither shock nor hypoxemia was evident.[3] Lactic acidosis that occurs without clinical evidence of tissue hypoperfusion is classified as type B.[2] In 1963 type B lactic acidosis was described in patients with acute leukemia.[4] Since then, various hematologic malignant neoplasms have been reported to cause lactic acidosis. In addition, lactic acidosis has also been noted to occur with solid tumors (breast, colon, lung), usually in the presence of liver or bone marrow metastases.[5] Type B lactic acidosis has not, to our knowledge, been previously described in patients with multiple myeloma.

Although the ultimate cause of lactic acidosis is an imbalance between lactate production and use, the mechanism in malignant disorders is controversial. Lactate production is largely determined by glycolytic activity.[6] It has been postulated that in patients with cancer, glycolytic flux is stimulated by ischemia due to a tightly packed neoplastic tissue bed or leukemic microemboli.[7] It is also possible that increased lactate production is caused by a primary increase in glycolytic activity in neoplastic tissue. The association between malignant disease and abnormalities of glucose metabolism was initially described in 1925.[8] In 1930 it was noted that malignant cells showed accelerated glycolytic activity with the production of lactic acid.[9] It was proposed that cancer cells had decreased respiration that caused the cells to increase their glycolytic rate to maintain adenosine triphosphate production. Later studies supported the observations of increased glycolytic activity but found that tissue oxygenation and respiratory activity in neoplastic cells were intact.[10] This primary increase in glycolytic activity has been called aerobic glycolysis.[10] The reason why malignant cells choose to satisfy their energy demands in this way is not clear. Glycolytic activity in cancer cells is much less responsive to feedback regulation and proceeds at a higher rate than required by the Krebs cycle.[6,9] This may confer advantage to malignant cells by promoting unrestrained growth.[10]

A human myeloma cell line was used to show that glycolytic flux and lactate production were increased by insulin and insulinlike growth factor-1 (IGF-1).[11] The ability of insulin and IGF-1 to stimulate glycolysis and lactate production in myeloma cells may relate to the fact that plasma cells are derived from the same germ layer as tissues traditionally considered to be insulin sensitive—liver, muscle, and fat.[11] It is not clear, however, why lactic acidosis has not been previously noted in patients with multiple myeloma. Possibly only rare myeloma cell lines are capable of increasing lactate production enough to overwhelm utilization pathways.

REFERENCES

1. Kopec IC, Groeger JS: Life-threatening fluid and electrolyte abnormalities associated with cancer. Crit Care Clin 1988; 4:81-105
2. Cohen RD, Woods HF: Clinical and Biochemical Aspects of Lactic Acidosis. Boston, Mass, Blackwell Scientific Publications, 1976
3. Huckabee WE: Abnormal resting blood lactate: 1. The significance of hyperlactatemia in hospitalized patients. Am J Med 1961; 30:833-839
4. Field M, Block JB, Rall DP: Lactic acidosis in acute leukemia (Abstr). Clin Res 1963; 11:193
5. Spechler SJ, Esposito AL, Koff RS, Hong WK: Lactic acidosis in oat cell carcinoma with extensive hepatic metastases. Arch Intern Med 1978; 138:1663-1664
6. Mizock BA: Lactic acidosis. Dis Mon 1989; 35:233-300
7. Block JB: Lactic acidosis in malignancy and observations on its possible pathogenesis. Ann NY Acad Sci 1974; 230:94-102
8. Cori CF, Cori GT: The carbohydrate metabolism of tumors. J Biol Chem 1925; 63:397-404
9. Warburg O: Metabolism of Tumors. London, Engl, Constable & Co, 1930
10. Weber G: Enzymology of cancer cells (2d of 2 pts). N Engl J Med 1977; 296:541-551
11. Freund GG, Kulas DR, Mooney RA: Insulin and IGF-1 increase mitogenesis and glucose metabolism in the multiple myeloma cell line, RPMI 8226. J Immunol 1993; 151:1811-1820

Hemorrhagic Fever With Renal Syndrome in California

WILLIAM MORRIS, MD, MPH
MOLLY FAINSTAT, MD
TRACEY ROBINSON, MD
ROBERT HOO, MD
San Jose, California

HANTAVIRUS DISEASE (HVD) encompasses the spectrum of illness caused by infection with viruses of the *Hantavirus* genus of Bunyaviridae.[1] Antibodies to hantaviruses have been demonstrated in human serum specimens throughout the world.[2] Until recently, hantavirus infection was thought either to be asymptomatic or to result in hemorrhagic fever with renal syndrome, an illness of varying severity characterized by fever, hypotension, acute renal failure, and thrombocytopenia.[3] The recent detection in the southwestern region of the United States of rising antibody titers to hantavirus in serum specimens from persons with unexplained acute respiratory failure shows that the clinical expression of hantavirus infection is broader than originally recognized.[4] Annually there are about 200,000 documented cases of hemorrhagic fever with renal syndrome worldwide, with nearly 50% of the cases in the People's Republic of China. Fewer cases occur in Korea, Russia, Scandinavia, Europe, and the Balkan region.[2] We describe a case of this illness confirmed in a California resident with a recent history of travel to Korea.

Report of a Case

The patient, a 30-year-old Korean man, was admitted because of nausea and vomiting associated with diffuse abdominal pain, headache, nonproductive cough, myalgias, and temperatures as high as 38.3°C (101°F), all of three days' duration. Four days before admission the patient had returned from a vacation to Korea. He had trav-

(Morris W, Fainstat M, Robinson T, Hoo R: Hemorrhagic fever with renal syndrome in California. West J Med 1994; 161:418-421)

From the Departments of Internal Medicine and Rheumatology, Santa Clara Valley Medical Center, San Jose, California. Dr Hoo is now with the Department of Anesthesiology, Loma Linda (California) Medical Center.

Reprint requests to William Morris, MD, MPH, 1818 Arbor Dr, San Jose, CA 95125.